

The mutein of the present invention may also have the coding sequence fused in frame to a marker sequence which allows for purification of the mutein of the present invention. The marker sequence may be a hexa-histidine tag or the T7 peptide (amino acid sequence: Met Ala Ser Met Thr Gly Gly Gln Gln Met Gly (SEQ ID NO:4)) supplied by a vector to provide for purification of the polypeptide fused to the marker in the case of a bacterial host, or, for example, the marker sequence may be a hemagglutinin (HA) tag when a mammalian host, e.g. COS-7 cells, is used. The HA tag corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson, I., *et al.*, *Cell* 37:767 (1984)). Other marker sequences well known to those skilled in the art may be used for similar purposes.

In the Claims:

Please add the following new claims 48-67:

48. (New) The mutein of claim 1, wherein said neutral amino acid is selected from the group consisting of serine, threonine, alanine, asparagine, glutamine, cysteine, and serine, and said hydrophobic amino acid is selected from the group consisting of tyrosine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine.

49. (New) The polynucleotide of claim 23, wherein said neutral amino acid is selected from the group consisting of serine, threonine, alanine, asparagine, glutamine, cysteine, and serine, and said hydrophobic amino acid is selected from the group consisting of tyrosine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine.

50. (New) A method for delivering a physiologically active mutein of human bFGF, or a biologically active peptide thereof, to an animal, comprising administering *in vivo* into a cell or a tissue of said animal a composition comprising

A) a polynucleotide encoding said physiologically active mutein, or a biologically active peptide thereof, wherein said polynucleotide is operably linked to a promoter, and

B) a pharmaceutically acceptable carrier,

wherein said physiologically active mutein comprises the substitution of a neutral and/or hydrophobic amino acid for one or more of the following:

(a) Glutamate 89; or

(b) Aspartate 101; or

(c) Leucine 137;

wherein the numbering of amino acids is based on SEQ ID NO:1; and wherein said physiologically active mutein, or a biologically active peptide thereof, has improved mitogenic agonist activity over wild-type basic fibroblast growth factor;

wherein said polynucleotide is taken up by the cells of said animal; and

wherein said polypeptide is expressed.

51. (New) The method of claim 50, wherein said physiologically active mutein of human bFGF, or a biologically active peptide thereof, comprises SEQ ID NO:3.

52. (New) The method of claim 50, wherein said promoter is selected from the group consisting of an LTR, a SV40, a CMV, a mouse metallothionein-I, a PGK, and an α -factor acid phosphatase promoter.

53. (New) The method of claim 50, wherein said polynucleotide further comprises an enhancer.

54. (New) The method of claim 53, wherein said enhancer is selected from the group consisting of an SV 40 enhancer, a cytomegalovirus early promoter enhancer, a polyoma enhancer on the late side of the replication origin, and an adenovirus enhancer.

55. (New) The method of claim 50, wherein said polypeptide further comprises a translation termination sequence.

56. (New) The method of claim 50, wherein the biological activity of said physiologically active mutein, or a biologically active peptide thereof, is detected as causing mitogenic agonist activity.

57. (New) The method of claim 50, wherein said animal is a mammal.

58. (New) The method of claim 50, wherein said cell or tissue is associated with a wound, ischemia, a heart disease, a peripheral vascular disease, a gastric ulcer, a duodenal ulcer, stroke, or a neural injury.

59. (New) A method for delivering a physiologically active mutein of human bFGF, or a biologically active peptide thereof, to an animal, comprising administering *ex vivo* into a cell or a tissue of said animal a composition comprising

A) a polynucleotide encoding said mutein of human bFGF, or a biologically active peptide thereof, wherein said polynucleotide is operably linked to a promoter, and

B) a pharmaceutically acceptable carrier,

wherein said physiologically active mutein comprises the substitution of a neutral and/or hydrophobic amino acid for one or more of the following:

- (a) Glutamate 89; or
- (b) Aspartate 101; or
- (c) Leucine 137;

wherein the numbering of amino acids is based on SEQ ID NO:1; and wherein said physiologically active mutein, or a biologically active peptide thereof, has improved mitogenic agonist activity over wild-type basic fibroblast growth factor;

wherein said cell or tissue is removed from said animal;

wherein said polynucleotide is introduced *in vitro* into said removed cell or tissue;

wherein a sufficient amount of time is given to allow incorporation of said polynucleotide into said removed cell or tissue;

wherein said polypeptide is expressed; and

wherein said removed cell or tissue is re-inserted into said animal.

60. (New) The method of claim 59, wherein said physiologically active mutein of human bFGF, or a biologically active peptide thereof, comprises SEQ ID NO:3.

61. (New) The method of claim 59, wherein said promoter is selected from the group consisting of an LTR, a SV40, a CMV, a mouse metallothionein-I, a PGK, and an α -factor acid phosphatase promoter.

62. (New) The method of claim 59, wherein said polynucleotide further comprises an enhancer.

63. (New) The method of claim 62, wherein said enhancer is selected from the group consisting of an SV 40 enhancer, a cytomegalovirus early promoter enhancer, a polyoma enhancer on the late side of the replication origin, and an adenovirus enhancer.

64. (New) The method of claim 59, wherein said polypeptide further comprises a translation termination sequence.

65. (New) The method of claim 59, wherein the biological activity of said physiologically active mutein, or a biologically active peptide thereof, is detected as causing mitogenic agonist activity.

66. (New) The method of claim 59, wherein said animal is a mammal.

67. (New) The method of claim 59, wherein said cell or tissue is associated with a wound, ischemia, a heart disease, a peripheral vascular disease, a gastric ulcer, a duodenal ulcer, stroke, or a neural injury.